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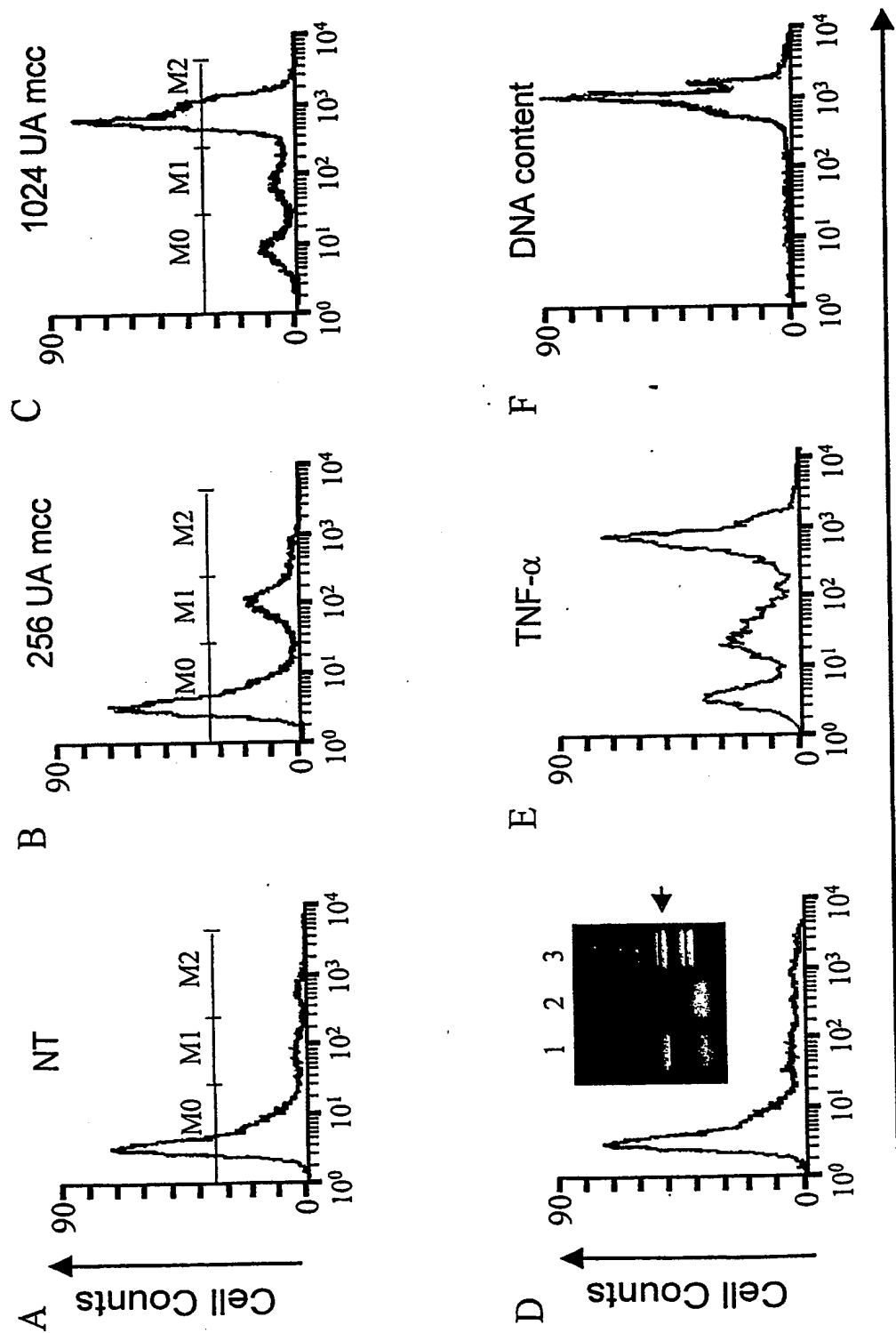
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For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: APOPTOGENIC-BACTERIOCINS COMBINING BROAD SPECTRUM ANTIBIOTIC AND SELECTIVE ANTI-TU-  
MORAL ACTIVITIES, AND COMPOSITIONS AND USES THEREOF

(57) Abstract: The present invention relates generally to bacterial proteins, particularly to . apoptogenic-bacteriocins, which are capable of killing other bacteria and of also inducing apoptosis in certain eukaryotic cells. The apoptogenic-bacteriocin of the present invention produces apoptosis in tumor-derived cells or cancer cells, while being not cytotoxic to normal cells and not inducing any evident toxicity *in vivo* in normal animals. Uses of the apoptogenic-bacteriocin and methods of treating cancer, tumors and other diseases of aberrant cell growth are provided.

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PI Fluorescence Intensity

FIGURE 1

**A**

Phase contrast

Nuclear staining

NT Control

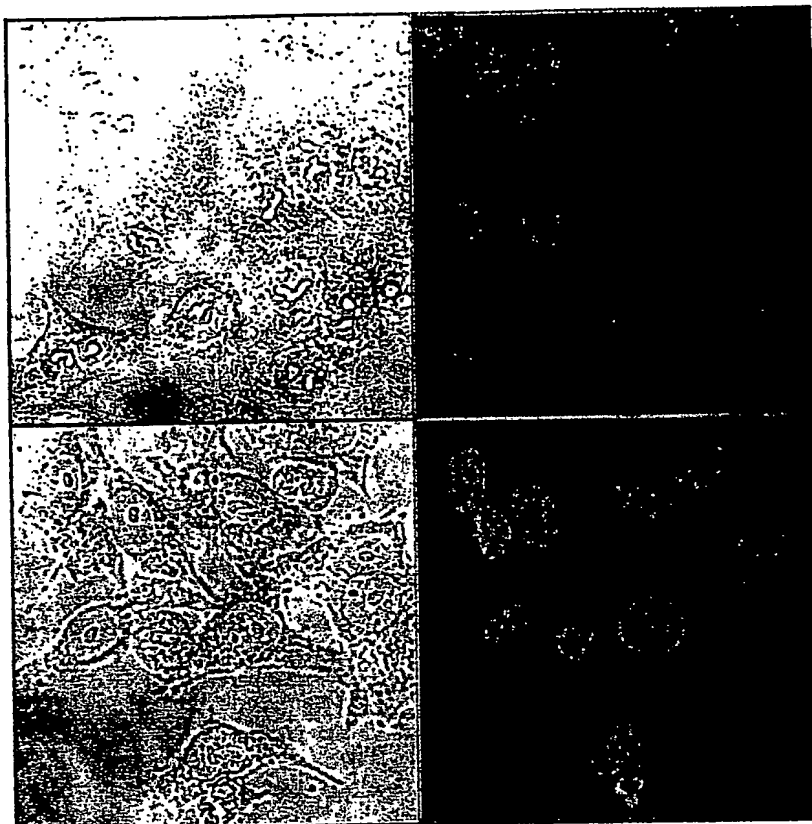
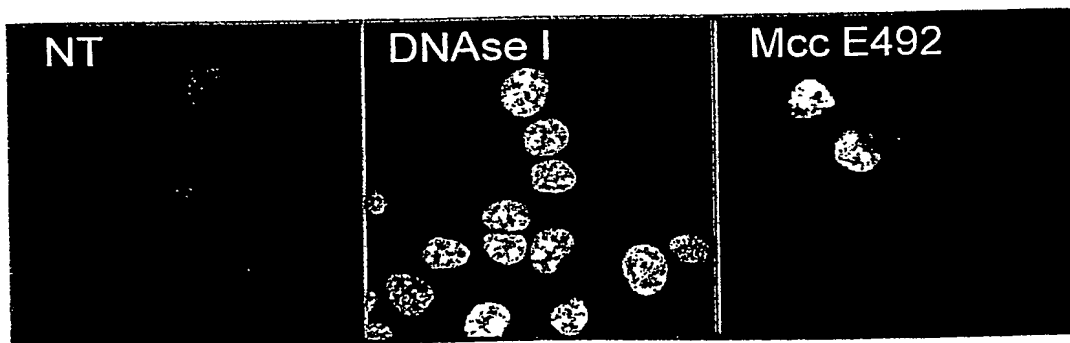
+ 512 AU  
mcc E492**B**

FIGURE 2

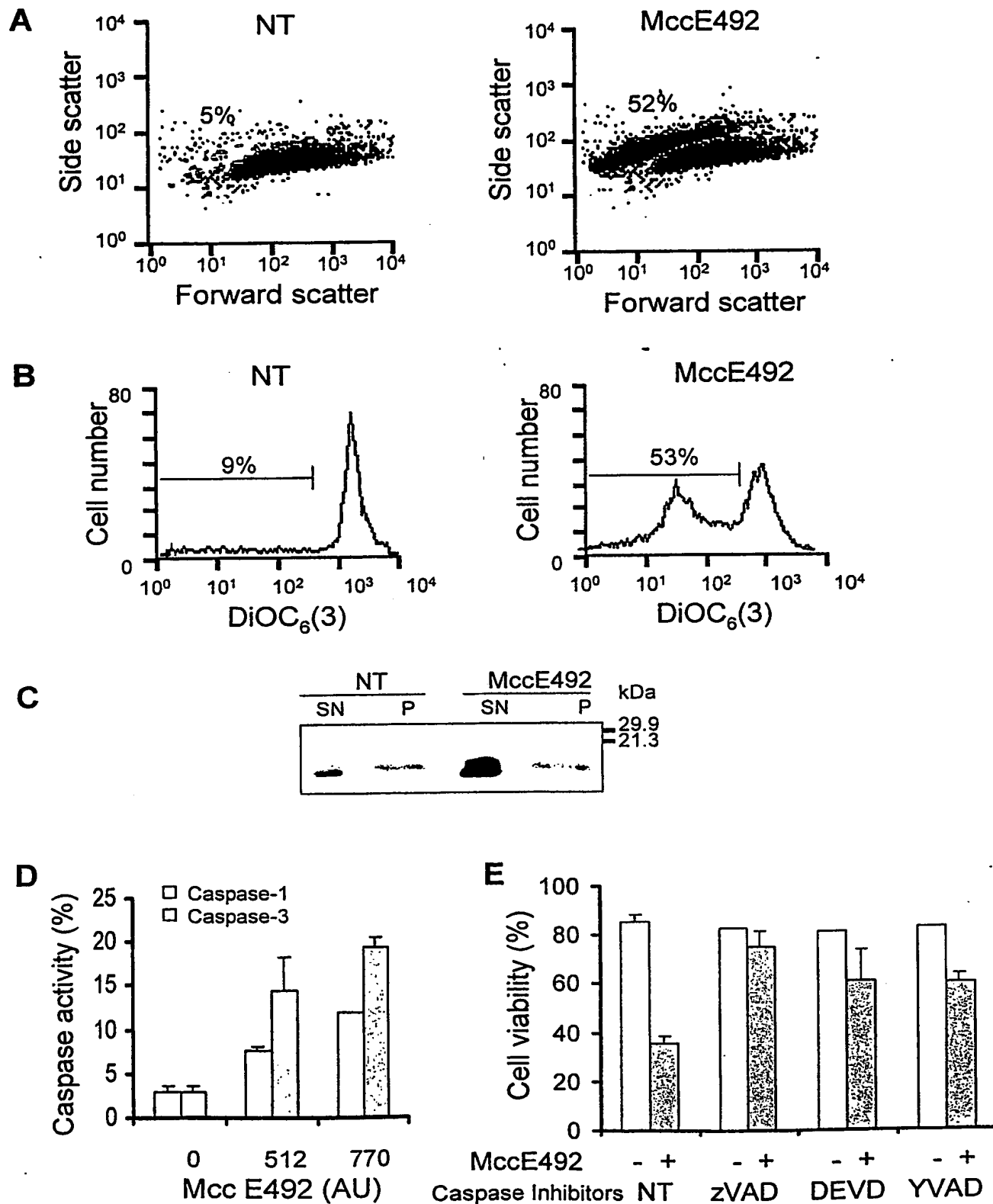


FIGURE 3

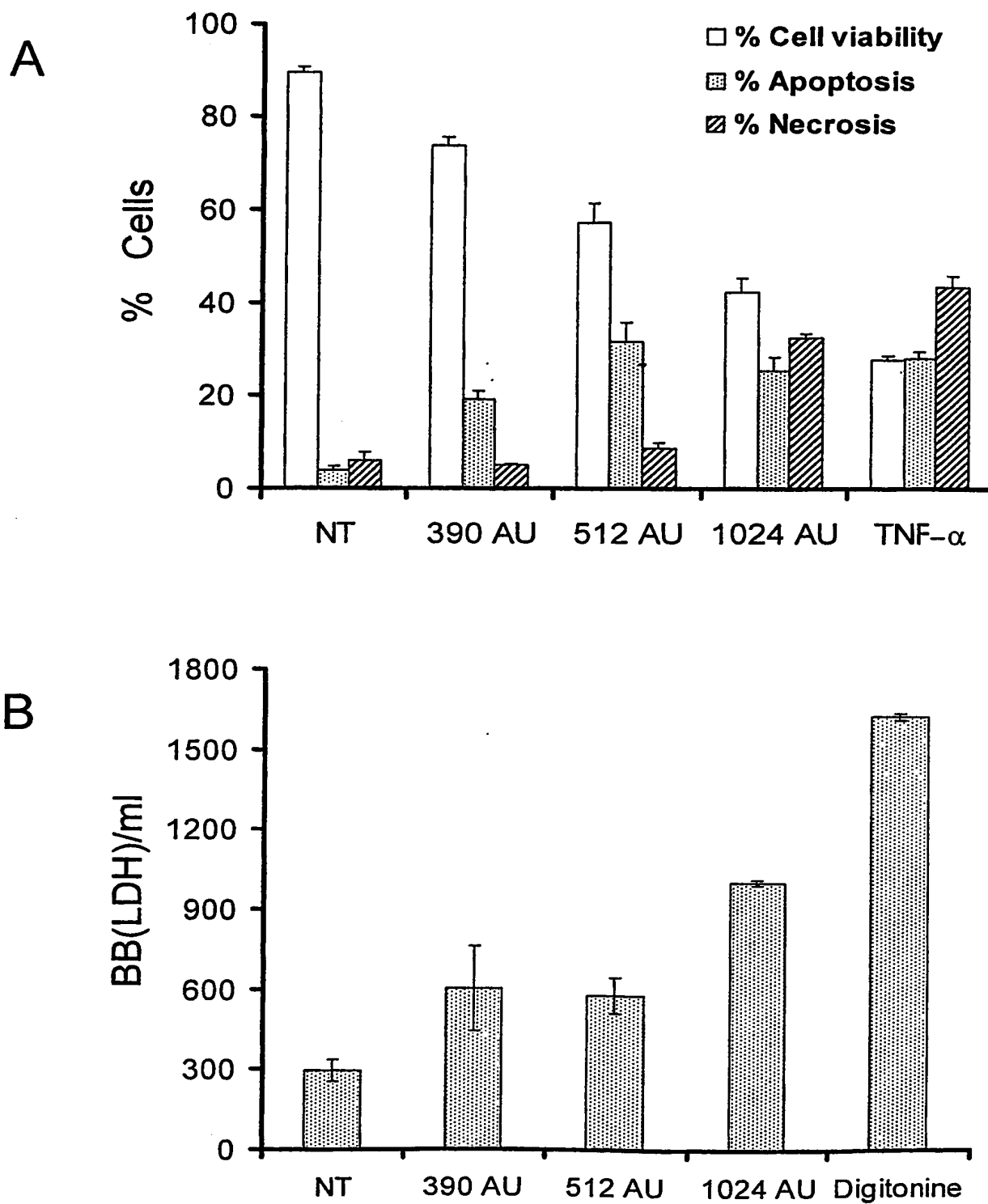


FIGURE 4

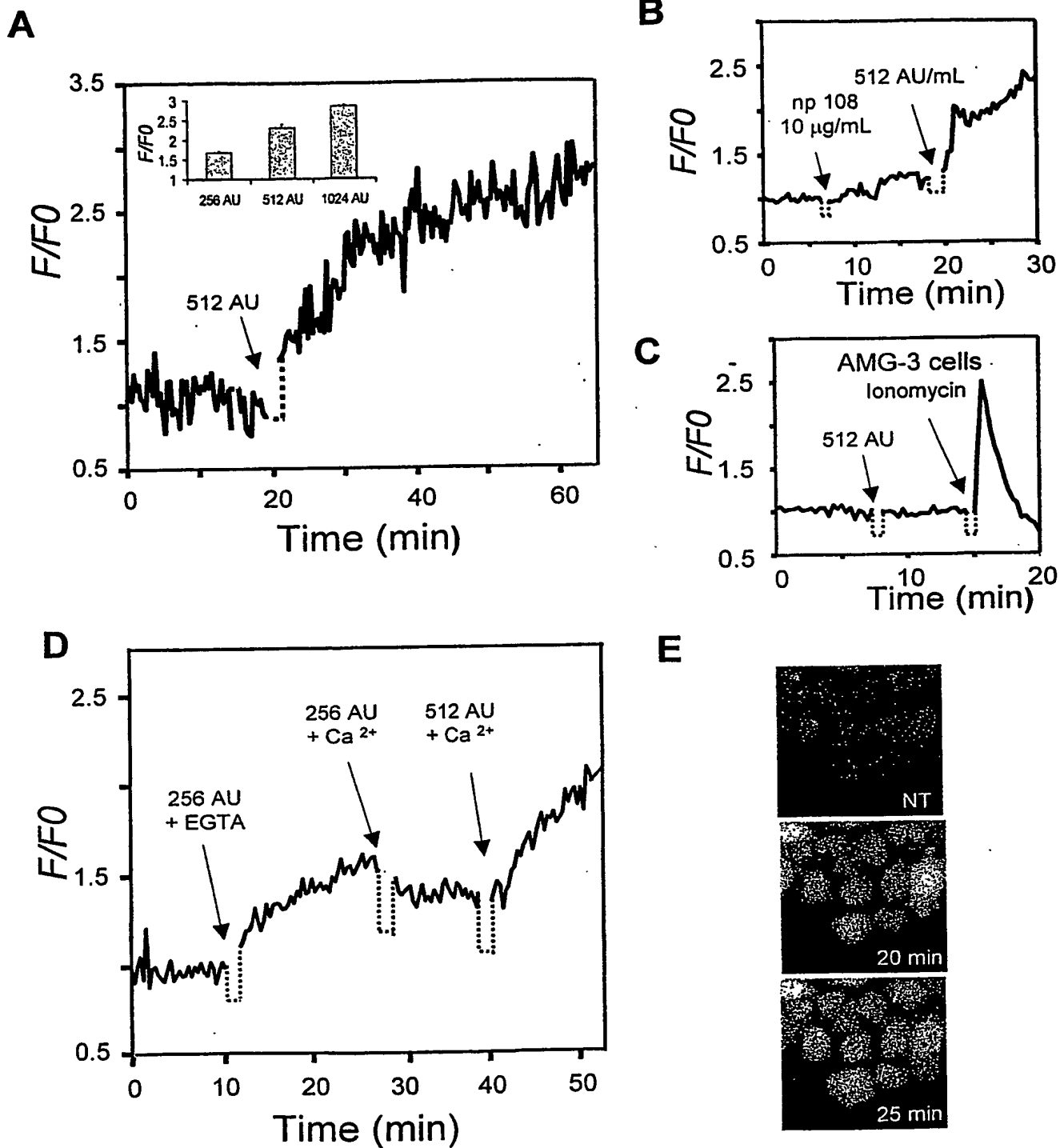


FIGURE 5

Best Available Copy

MELRMREISQKDLNLAFGAG  
ETDPNTQLLNDLGNNMAWGA  
ALGAPGGLGSAALGAAGGAL  
QTVGQGLIDHGPVNVPIPVL  
IGPSWNGSGSGYNSATSSSG  
SGS

FIGURE 6

GETDPNTQLLNDLGNNMAWG  
AALGAPGGLGSAALGAAGGA  
LQTVGQGLIDHGPVNVPIPV  
LIGPSWNGSGSGYNSATSSS  
GSGS

FIGURE 7



↓  
MYMRELDREELNCVGGAGDP  
LADPNSQIVRQIMSNAAWGP  
PLVPERFRGMAVGAAGGVTQ  
TVLQGAAAHMPVNVPIPKVP  
MGPSWNGSKG

FIGURE 8

# INTERNATIONAL SEARCH REPORT

International Publication No.  
PCT/IB 00821

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/26 C12N15/31 C12N15/63 A61K38/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EMBL, EMBASE, EPO-Internal, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LAGOS ROSALBA ET AL: "Identification and properties of the genes encoding microcin E492 and its immunity protein." JOURNAL OF BACTERIOLOGY, vol. 181, no. 1, January 1999 (1999-01), pages 212-217, XP002251274 ISSN: 0021-9193 the whole document	1-11
X	-& DATABASE EMBL 'Online! 16 October 2001 (2001-10-16) retrieved from EBI Database accession no. Q9Z4N4 XP002251278 abstract	1-11

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*Z\* document member of the same patent family

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14 August 2003

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# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/IB 00821

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>HETZ CLAUDIO ET AL: "Microcin E492, a channel-forming bacteriocin from <i>Klebsiella pneumoniae</i>, induces apoptosis in some human cell lines."</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 99, no. 5, 5 March 2002 (2002-03-05), pages 2696-2701, XP002251275  <a href="http://www.pnas.org">http://www.pnas.org</a> March 5, 2002                      ISSN: 0027-8424                      the whole document</p> <p>-----</p>	1-11

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB 03/00821

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/IB 03 00821

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-11 all partially

The isolated bacterial apoptogenic bacteriocin, microcin E492 fromn Klebsiella pneumoniae

Invention 2: claims 1-11 all partially

The isolated bacterial apoptogenic bacteriocin, microcin 24 from E. coli

Invention 3: claims 12-21

A method for apoptosis of tumour cells, cancer cells or cells undergoing aberrant growth in a mammal comprising administering to said mammal an effective amount of an apoptogenic bacteriocin.